Research Article

Transition Metal Complexes of Knoevenagel Condensate- β- Ketoesters with S-Methyl Dithiocarbazate- Synthesis and Characterisation

***P. Yogalakshmi[1], Dr. Chitra Subramanian[2]**
1. Department of Chemistry, G Venkatasamy Naidu College, Kovilpatti, Tamil Nadu, India.
2. Department of Chemistry, PSGR Krishnammal College, Coimbatore, Tamil Nadu, India.
***Corresponding author's E-mail:** s.dharu1996@yahoo.com

Received: 09-09-2017; **Revised:** 05-06-2018; **Accepted:** 14-09-2018.

ABSTRACT

New Knoevenagal - β-ketoester condensate Schiff bases [(HPOB--(HSMD)$_2$,HEOA--(HSMD)$_2$] and [(HMOA---(HSMD)$_2$] were prepared by reaction of S-Methyl dithiocarbazate with Knoevenagal - β-ketoester derived from 1-hydroxy benzaldehyde and N-phenyl-2-oxobutanamide (HPOB), ethylester of 3-oxobutanoic acid (HEOA) and methyl ester of 3-oxobutanoic acid (HMOA).The ligands behave as a dinegatively charged tetradentate N_2S_2 chelating agent producing stable crystalline complexes of the general formula [ML] where M = Cu $^{2+}$,Co^{2+},Ni^{2+},Cd^{2+} and Zn^{2+} and L = HPOB-(HSMD)$_2$,HEOA-(HSMD)$_2$ and HMOA-(HSMD)$_2$. The new complexes obtained have been characterised on the basis of their analytical, spectroscopic, conductivity and magnetic moment data. The data support a four coordinated structure for the complexes. Free ligands and their metal complexes have been screened for their antimicrobial activity on different species of pathogenic bacteria and fungi and their biological activity is discussed briefly.

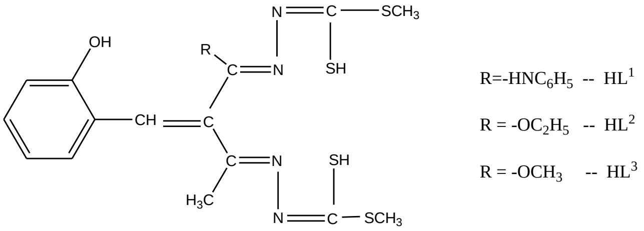
Keywords: Knoevenagal- β- ketoester condensate, S- Methyl dithiocarbazate, Schiff base complexes- preparation- characterisation, anti-bacterial, anti- fungicidal study.

INTRODUCTION

The coordination complexes of 2,4-pentanedione and its derivative ligands are shown considerable interest over few decades. The enolic proton of the predominantly existing enol form of 2,4-pentane dione undergoes dissociation to form a number of complexes with metal ions. Condensing the active methylene group of the 2, 4-pentane dione with aldehyde can prohibit the formation of the enol tautomer called Knoevenagal condensation.[1-3] The Knoevenagal condensation reaction is a useful reaction in organic synthesis that has been employed for carbon-carbon bond formation. It is usually performed in organic solvents in presence of common bases and their salts. [4] A number of catalysts have been used for the Knoevenagal condensation.[5-20] However these methods have some limitations, such as using hazardous solvents, high catalyst loading or nonrecoverable catalysts that sometimes contain some toxic metals.

Metal complexes of bidentate Schiff base ligands in which the donor atoms are N and S (NS- donor set) have been studied extensively. The marked alteration in carcinostatic and antiviral activity of metal chelates due to minor change of the ligand led to synthesise and characterise a number of N-S donor ligands. [21-24]

Similarly large amount of work has been done on metal complexes of S-substituted esters of dithiocarbazic acid. The survey of literature reveals that though metal complexes of bi-, tri-, and tetra dentate sulphur-nitrogen chelating agents have been reported, no work has been carried out on the synthesis of Schiff base utilising Knoevenagal condensation with S-substituted esters of dithiocarbazic acid. The Schiff bases formed by the above combination led to the formation of the following types of ligands having four coordination sites having the formulae HPOB---(HSMD)$_2$, HEOA---(HSMD)$_2$ and HMOA---(HSMD)$_2$ and metal complexes of these ligands are discussed herein.



MATERIALS AND METHODS

All the reagents used were of Analytical grade. ^{1}H NMR, ^{13}C NMR and elemental analyses were carried out in STIC, Cochin. The IR spectra were recorded in KBr pellets in the range 4000– 400 cm^{-1}. The electronic spectra were recorded from chloroform solution with a Hitachi Perkin Elmer 20/200 recording spectrophotometer in the range 800-200 nm. Melting points were recorded with a Boetius micro heating table and were uncorrected**.** The molar conductance of the complexes was measured in DMSO solutions using 305 systronic conductivity bridges. Magnetic susceptibility measurements were carried out using Guoy balance**.** The starting compounds were prepared by methods reported in the literature.

A. Synthesis of s-methyl dithiocarbazate: ($C_2H_6N_2S_2$)

This compound is prepared by the method of Bahr and Schleitzer.[25]

Potassium hydroxide (11.4g) was completely dissolved in 9:1 alcohol-water mixture (50ml) and the mixture was cooled in ice. To the cooled solution hydrazine hydrate (10g) was added slowly with stirring. A solution of carbon disulphide (15.2 g) in alcohol (125 mL) was then added drop wise from a burette with constant stirring, over a period of 1 h. The temperature of the mixture was kept below 10˚C during the addition. The resulting yellow oil was separated by means of a separating funnel and dissolved in 2:3 alcohol –water mixture and this solution was cooled in ice. Methyl iodide (29 g) was added slowly with vigorous mechanical stirring; after the addition, the mixture was stirred for further 10 min. while a white product separated. Ice-cold water (50 mL) was then added and the stirring was continued for another 10 min. The product is separated, filtered, washed with water and dried in air and crystallized from benzene (75 mL).

B. Synthesis of Knoevenagal Condensate β-diketoester: $(C_{11}H_9O_3R)(R=OCH_3,OC_2H_5,NHC_6H_5)$

The Knoevenagal condensate β--ketoesters (HMOA/HEOA/HPOB) were prepared by the following procedure:[26]

Equimolar quantity of 1-hydroxy- benzaldehyde and β – ketoester (methyl ester of 3 - oxobutanoic acid, ethyl ester of 3 - oxobutanoic acid, N - phenyl - 2 - oxo butanamide) were taken in a 100 mL conical flask and cooled for 1h under freezing mixture. After cooling the solution, 1 mL of piperidine was added dropwise with constant stirring. The mixture was kept under freezer for 24 h, the product separated was filtered and recrystallised in ethanol.

C. Synthesis of Schiff Base Ligands: $(C_{15}H_{17}N_4OS_4R)(R=OCH_3,OC_2H_5,NHC_6H_5)$

The Schiff base ligands were prepared as follows: S-methyl dithiocarbazate dissolved in alcohol (2 mol) was added to a solution of Knoevenagal condensate of β-ketoester (1 mol) in ethanol, the mixture was heated under reflux for 30 min and then left to stand for slow cooling. The product was separated, recrystallised from chloroform.[27]

D. Synthesis of Copper Complexes: $(C_{15}H_{15}N_4S_4ORCu)(R=OCH_3,OC_2H_5,NHC_6H_5)$

An ethanolic solution(10 mL) of Knoevenagal β- keto ester Schiff base (HMOA-$(HSMD)_2$), (HEOA-$(HSMD)_2$ and (HPOB-$(HSMD)_2$ (1 mol) was stirred with ethanolic solution(10ml) of copper(II) chloride (1 mol)and the stirring is continued for 5 h. and heated on a hot plate for 10 min.. The product was separated and washed with ethanol.

E. Synthesis of Nickel(II) Complexes: $(C_{15}H_{15}N_4S_4ORNi)(R=OCH_3,OC_2H_5,NHC_6H_5)$

An ethanolic solution(10ml) of Knoevenagal β- keto ester Schiff base(HMOA-$(HSMD)_2$),(HEOA--$(HSMD)_2$ and (HPOB--$(HSMD)_2$ (1 mol) was stirred with ethanolic solution(10 mL) of nickel(II) chloride (1 mol) and the stirring was continued for 5 h. and heated on a hot plate for 10 min. The product was separated, washed with ethanol.

F. Synthesis of Cobalt (II) Complexes: $(C_{15}H_{15}N_4S_4ORCo)(R=OCH_3,OC_2H_5,NHC_6H_5)$

An ethanolic solution(10 mL) of Knoevenagal β- keto ester Schiff base(HMOA--$(HSMD)_2$), (HEOA--$(HSMD)_2$ and HPOB--$(HSMD)_2$ (1 mol) was stirred with ethanolic solution(10 mL) of cobalt(II) chloride (1 mol) and the stirring was continued for 5 h. and heated on a hot plate for 10 min. The product was separated, washed with ethanol.

G. Synthesis of Cadmium(II) Complexes: $(C_{15}H_{15}N_4S_4ORCd)$ $(R=OCH_3,OC_2H_5,NHC_6H_5)$

An ethanolic solution(10ml) of Knoevenagal β- keto ester Schiff base (HMOA--$(HSMD)_2$), (HEOA--$(HSMD)_2$ and HPOB---$(HSMD)_2$ (1 mol) was stirred with ethanolic solution (10 mL) of cadmium(II) chloride (1mol) and the stirring was continued for 5 h. and heated on a hot plate for 10 min. The product was separated, washed with ethanol.

H. Synthesis of Zinc(II) Complexes: $(C_{15}H_{15}N_4S_4ORZn)(R=OCH_3,OC_2H_5,NHC_6H_5)$

An ethanolic solution(10ml) of Knoevenagal β- keto ester Schiff base (HMOA--$(HSMD)_2$), (HEOA--$(HSMD)_2$ and (HPOB---$(HSMD)_2$ (1 mol) was stirred with ethanolic solution (10 mL) of zinc(I) chloride (1mol) and the stirring was continued for 5 h. and heated on a hot plate for 10 min. The product was separated, washed with ethanol.

I. Microbiocidal Assay

Antibacterial and antifungal activities of the ligands and their complexes were tested *in vitro* against two bacterial and two fungal species using disc diffusion method. Both the bacteria and fungi were cultivated on Muller Hinton agar (MHA) and Sabouards dextrose sugar medium respectively.

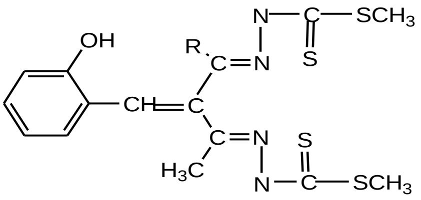
The degree of bactericidal and fungicidal activities were determined by measuring diameter of inhibition zone and compared with the standard drug ciprofloxacin and flucanazol respectively.

The bactericidal activity was carried out by preparing the Petri dish plates with Muller Hinton agar medium. The overnight fresh culture was inoculated in the plates with the help of sterile cotton swab. The discs were placed on the respective places along with the standard and soaked with the extract solution overnight. The plates were incubated at 37^{0}C for 24 h and the zone of inhibition was measured by zone reader.

In the same way the fungicidal activity was carried out with Sabouards dextrose sugar medium and the plates were incubated at 28^{0}C for 48 h and the zone of inhibition was measured by zone reader. Compounds that showed positive antimicrobial activity with the disc diffusion assay were subjected to the Broth Dilution method by Kirby-Bauer procedure for the quantitative measurement of microstatic (inhibitory) activity. The lowest concentration which completely inhibited visible microbial growth was recorded as the minimum inhibitory concentration (MIC, µg/mL**)**.

RESULTS AND DISCUSSION

The Knoevenagal β- keto ester Schiff base (Ia-thione form) has proton adjacent to the thione group and consequently it can remain either as the thione form (Ia) or as the thiol form (Ib) or as a tautomeric equilibrium mixture of both the thione and thiol forms. As it is relatively unstable in the monomeric thione form, it tends to turn to a stable C-S single bond in the presence of metal ions by enethiolization with the concomittant formation of metal complexes of the deprotonated form of the ligands. [28, 29] So the ligands might be expected to behave as binegatively charged tetradentate by coordinating a metal ion through the two thiolosulphur atoms and two azomethine nitrogen atoms. The results discussed below support that the ligands do behave in the same way.

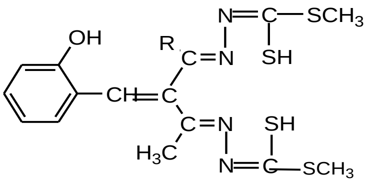


R=-HNC$_6$H$_5$ -- HL^1

R = -OC$_2$H$_5$ -- HL^2

R = -OCH$_3$ -- HL^3

(Ia)



R=-HNC$_6$H$_5$ -- HL^1

R = -OC$_2$H$_5$ -- HL^2

R = -OCH$_3$ -- HL^3

(Ib)

The elemental analyses for all the compounds (Table I) are found to be in good agreement with the above molecular formulae.

Table I: Physical characterisation and analytical data of the complexes:

Compound	Empirical Formula	Yield %	M.p/ decomp* (ºC)	Colour	Found (Calculated)			
					C %	H %	N %	S %
HL^1	HPOB--(HSMD)$_2$ $C_{21}H_{23}N_5OS_4$	80	>180	Orange	50.93 (51.72)	4.21 (4.34)	14.01 (14.36)	25.03 (26.29)
HL^2	HEOA-(HSMD)$_2$ $C_{17}H_{22}N_4O_2S_4$	85	>185	Orange	38.96 (39.40)	3.97 (4.25)	13.05 (13.13)	29.68 (30.06)
HL^3	HMOA-(HSMD)$_2$ $C_{16}H_{20}N_4O_2S_4$	75	>180	Orange	46.41 (46.34)	4.38 (4.57)	11.90 (12.71)	18.56 (29.10)
Cu L^1	[HPOB-(SMD)$_2$]Cu $C_{21}H_{21}$ O N_5 S_4Cu	80	>190	Brown	45.70 (45.76)	3.80 (3.84)	12.65 (12.71)	23.21 (23.26)
Cu L^2	[HEOA-(SMD)$_2$]Cu $C_{17}H_{20}$ $O_2N_4S_4$Cu	85	>190	Brown	39.98 (40.50)	3.95 (3.99)	11.09 (11.11)	25.31 (25.44)
Cu L^3	[HMOA-(SMD)$_2$]Cu $C_{16}H_{18}$ $O_2N_4S_4$Cu	93	180.6	Brown	39.11 (39.21)	3.67 (3.70)	11.33 (11.43)	25.15 (26.16)
Ni L^1	[HPOB-(SMD)$_2$]Ni $C_{21}H_{21}$O N_5S_4 Ni	95	179	Brown	45.09 (46.17)	3.96 (3.87)	12.55 (12.82)	22.68 (23.47)
Ni L^2	[HEOA-(SMD)$_2$] Ni $C_{17}H_{20}$ $O_2N_4S_4$ Ni	93	>180	Brown	39.56 (40.89)	3.98 (4.04)	11.56 (11.22)	26.23 (25.68)
Ni L^3	[HMOA-(SMD)$_2$]Ni $C_{16}H_{18}$ $O_2N_4S_4$ Ni	95	>190	Brown	38.55 (39.60)	3.58 (3.74)	11.02 (11.50)	25.98 (26.42)
Co L^1	[HPOB-(SMD)$_2$]Co $C_{21}H_{21}$ O N_5 S_4Co	96	>190	green	45.99 (46.14)	3.57 (3.87)	12.57 (12.81)	22.92 (23.46)
Co L^2	[HEOA-(SMD)$_2$]Co $C_{17}H_{20}$ $O_2N_4S_4$Co	97	>190	Brown	39.55 (40.87)	3.92 (4.04)	10.55 (11.22)	25.02 (25.67)
Co L^3	[HMOA-(SMD)$_2$]Co $C_{16}H_{18}$ $O_2N_4S_4$Co	90	>190	Brown	38.56 (39.58)	3.56 (3.73)	10.96 (11.53)	25.32 (26.41)
Cd L^1	[HPOB-(SMD)$_2$]Cd $C_{21}H_{21}$ O N_5 S_4Cd	88	186	Yellow	41.03 (42.03)	3.25 (3.52)	10,98 (11.67)	22.03 (21.37)
Cd L^2	[HEOA-(SMD)$_2$]Cd $C_{17}H_{20}$ $O_2N_4S_4$Cd	86	185	Yellow	36.25 (36.91)	3.55 (3.65)	09.76 (10.13)	22.56 (23.19)
Cd L^3	[HMOA-(SMD)$_2$]Cd $C_{16}H_{18}$ $O_2N_4S_4$Cd	95	175	Yellow	36.01 (35.65)	3.26 (3.36)	10.11 (10.39)	23.46 (23.79)
Zn L^1	[HPOB-(SMD)$_2$]Zn $C_{21}H_{21}$ O N_5 S_4Zn	92	178	Orange Yellow	45.02 (45.61)	3.48 (3.83)	12.30 (12.66)	22.98 (23.18)
Zn L^2	[HEOA-(SMD)$_2$] Zn $C_{17}H_{20}$ $O_2N_4S_4$ Zn	91	176	Yellow	40.12 (40.35)	3.56 (3.98)	10.89 (11.07)	24.96 (25.34)
Zn L^3	[HMOA-(SMD)$_2$]Zn $C_{16}H_{18}$ $O_2N_4S_4$ Zn	90	>190	Yellow	38.68 (39.06)	3.55 (3.69)	10.98 (11.38)	25.87 (26.07)

*decomp = decomposition temperature

Table II: Infra-red, electronic spectral and molar conductance data for new Schiff base complexes

S.No	Compound	C=O	C-N	M-O	M-N	λ_m ohm^{-1} cm^2 mol^{-1}	λ_{max}
1	HPOB—(HSMD)$_2$	1707	1598	-	-	----	-
2	[HPOB-(SMD)$_2$]Cu	-	1604	540	455	2.1	307,410
3	[HPOB-(SMD)$_2$]Co	-	1612	563	463	1.1	360.5,454.5
4	[HPOB-(SMD)$_2$]Cd	-	1604	663	532	3.6.	
5	[HPOB-(SMD)$_2$]Ni	-	1604	547	486	1.8	411.5
6	[HPOB-(SMD)$_2$]Zn	-	1604	540	470	3.7	
7	HEOA-(HSMD)$_2$	1742	1609	-	-	--	-
8	[HEOA-(SMD)$_2$]Cu	-	1597	540	455	2.0	307,391
9	[HEOA-(SMD)$_2$]Co	-	1604	555	455	1.9	359,369.5, 454.5
10	[HEOA-(SMD)$_2$]Cd	-	1597	594	478	2.1	
11	[HEOA-(SMD)$_2$] Ni	-	1589	594	501	3.8	466.5
12	[HEOA-(SMD)$_2$] Zn	-	1604	524	455	1.0	
13	HMOA-(HSMD)$_2$	1735	1612	-	-	--	-
14	[HMOA-(SMD)$_2$]Cu	-	1604	540	470	1.5	331,408
15	[HMOA-(SMD)$_2$]Co	-	1597	524	478	1.4	364.5,382,454
16	[HMOA-(SMD)$_2$]Cd	-	1604	540	470	1.3	
17	[HMOA-(SMD)$_2$]Ni	-	1597	532	478	3.2	361
18	[HMOA-(SMD)$_2$]Zn	-	1604	540	478	3.9	-

The magnetic susceptibility values of all the complexes at room temperature are consistent with that of square planar geometry around the central metal ion.

IR Spectra

The IR spectra of the ligands do not show a band at 1720 cm^{-1} characteristic of >C=O which confirms the formation of Knoevenagal ester condensate and also the band at 2450-2600 cm^{-1} characteristic of –SH group is not seen suggesting that in the solid state ,Schiff bases remain in the thioketoform (Ia), but in solution it may remain as equilibrium mixture of both the thioketo (Ia) and thiol (Ib) tautomeric forms.[30] The deprotonation of α-NH is indicated by the appearance of a γ(C=N)b and at 1597–1612 cm^{-1} which confirms the complex formation. The coordination of the azomethine nitrogen atom and sulphur of thiol form which is indicated by appearance of new bands for M-O and M-N bands in the complexes (Table- II). The IR spectra of the complexes show broad band in the region 3000-3500 cm $^{-1}$ indicating that the phenolic –OH group in the salicylaldehyde moiety is not involved in the coordination. The possibility of α-nitrogen coordination is ruled out because of considerable strain. Ali and Livingstone have established that in the cases of S-methyl dithiocarbazate and its various Schiff bases that the thioether sulphur does not coordinate to the metal ion.[31] However IR spectroscopy may not be a sufficient tool because it is difficult to distinguish between a γ(O-H) and γ(N-H) so ^{1}HNMR is used to distinguish between them.

Electronic Spectral Studies

The electronic absorption spectra of the Schiff bases Cu(II), Ni(II), Co(II), Cd(II) and Zn(II) complexes were recorded at 300 K. The solvent absorption region assignment are given in Table II. These values are comparable with that of the other reported complexes.

In the absence of X-ray diffraction studies, the electronic spectra can be used in the determination of the structure of metal complexes as the number and position of spectral bands provide information about the geometry of the metal complexes.

The copper(II) complexes are said to possess square planar geometry. Since, the copper ion has been found to be reluctant to take up a regular tetrahedral geometry.[32,33] The absorption spectra of copper(II) complexes consist of intense band centered at 307-331cm^{-1} is attributed to $n \rightarrow \pi^*$ transition of azomethine group. The band at 391-410cm^{-1} is indicative of $^2B_{1g} \rightarrow {}^2A_{1g}$ which is in conformity to a square planar geometry.[34,35]

The electronic spectra of nickel(II) complexes occur below 600 nm. A lack of any electronic transition at longer wavelength is consistent with square planar geometry of nickel(II) compounds. Hence they can be clearly distinguished from octahedral and tetrahedral complexes. The obtained values are of particular importance since they were highly dependent on the geometry of the molecule. Thus the smaller value the wavelength of the band corresponding to the transition is resemblance between the geometry of the complex and that of square planar complex.[36, 37, 38]

The electronic spectra of cobalt(II) complexes show a band at 454 cm^{-1} which correspond to $d \rightarrow \pi^*$ MLCT (combination of $^2B_{1g} \rightarrow {}^2A_{1g}$ and $^1B_{1g} \rightarrow$ 2A1g transition).[39, 40, 41] The Cadmium (II) and Zinc (II) complexes with an electronic configuration of d^{10} did not show any d-d transition.

Molar Conductivity Studies

Molar conductivity (λ_m) measurements of the complexes were carried out using DMSO as the solvent at the concentration of 10^{-3}M indicate non-electrolyte behaviour of the complexes and conductivity values are found in the range 1.1-3.9 ohm^{-1} cm^2 mol^{-1}. Thus the complexes may be formulated as [ML] where M = Cu^{2+},Co^{2+},Ni^{2+},Cd^{2+} and Zn^{2+} and L = HPOB-$(HSMD)_2$,HEOA-$(HSMD)_2$ and HMOA-$(HSMD)_2$.

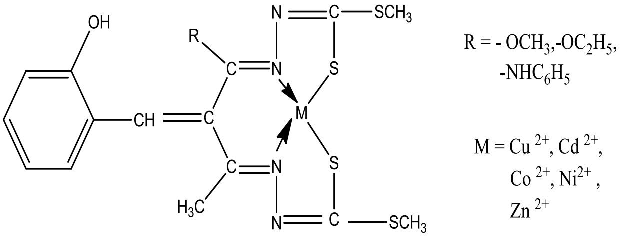
^{1}H and ^{13}C NMR

The ^{1}H NMR and ^{13}C NMR spectra of the [HPOB-$(SMD)_2$]Co (CoL^1) were recorded in DMSO-d_6 at room temperature. The results are given as below:

In ^{1}H NMR spectrum in one of the complexes of cobalt, the peak at 2.539 ppm can be ascribed to the $-SCH_3$ protons[42] and no signal is seen around 4.00 ppm as well as at 9.60 ppm which is the characteristic region of –S-H proton and –N-H protons which shows that thiol form of Schiff base is not present in DMSO solution and in presence of metal ion, enolization of the Schiff base was found to be greatly enhanced with the concomittant formation of cobalt complexes of the deprotonated form of the ligand. The existence of peak at 13.323 ppm confirms the presence of phenolic protons.

In ^{13}C NMR spectrum in one of the complexes of cobalt, the signal for >C=N (azomethine) carbon appears at δ144.698 ppm which confirms the complexation. The >C=S (thiolo) group signal is seen at δ154.617ppm.This indicates the participation of thiol group in bonding. Thus considerable shifts in carbon attached to S and N indicate the involvement of sulphur and nitrogen in coordination with cobalt atom.[43]

Thus on the basis of the above spectral evidences, tetra-coordinated structures may be proposed for the metal complexes as shown in the following scheme:



Biological Screening Study

The *invitro* biological screening effects of the investigated compounds were tested against two bacteria: *Staphylococcus aureus*, *Escherichia coli* and two fungi *Candida albicans* and *Aspergillus niger*. The measured zone of inhibition against the growth of various microorganisms is listed in Table III.

Table III: Quantitative antimicrobial assay results (Zone of growth inhibition) of the Schiff base ligands and related complexes

Micro Organism	Zone of growth inhibition (mm)																		
	Main compounds																		
	Std*	H L^1	Cu L^1	Ni L^1	Co L^1	Cd L^1	Zn L^1	H L^2	Cu L^2	Ni L^2	Co L^2	Cd L^2	Zn L^2	H L^3	Cu L^3	Ni L^3	Co L^3	Cd L^3	Zn L^3
S.aureus	30	12	16	18	09	12	11	12	18	13	13	12	14	14	18	12	14	15	13
E.coli	22	12	19	14	10	17	09	12	15	14	11	12	18	12	18	10	11	14	11
C.albicans	32	20	23	28	16	14	11	15	20	18	10	16	20	15	15	19	12	20	09
A.niger	32	17	30	21	20	20	13	20	20	15	-	15	18	22	12	18	11	20	15

*Ciprofloxacin for bacteria: *Flucanazol for fungi

Table IV: Quantitative antimicrobial assay results (MIC) of the Schiff base ligands and related complexes

Micro organism	Minimum Inhibitory Concentration (μg/mL)																	
	Main compounds																	
	H L^1	Cu L^1	Ni L^1	Co L^1	Cd L^1	Zn L^1	H L^2	Cu L^2	Ni L^2	Co L^2	Cd L^2	Zn L^2	H L^3	Cu L^3	Ni L^3	Co L^3	Cd L^3	Zn L^3
E.coli	125	125	62.5	62.5	62.5	125	250	62.5	250	125	125	62.5	125	250	125	125	125	125

Antimicrobial screening data reveal that the toxicity of metal chelates has increased considerably as compared to the parent ligands against the same microorganisms and under identical experimental conditions which indicate that the metal complexes exhibit higher antimicrobial activity than that of the free ligands. This is probably due to the greater lipophilic nature of the complexes. Such increased activity of the metal chelates can be explained on the basis of Overtone's concept[44] and Chelation theory.[45] According to Overtone's concept of cell permeability the lipid membrane that surrounds the cell favours the passage of only lipid soluble materials due to which liposolubility is an important factor which controls the antimicrobial activity. On chelation, the polarity of metal ion will be reduced to a greater extent due to the overlap of the ligand orbital and partial sharing of positive charge of metal ion with donor groups. Further, it increases the delocalization of π-electrons over the whole chelate ring and enhances the lipophilicity of the complex. This increased lipophilicity enhances the penetration of the complexes into lipid membrane and blocks the metal binding sites on enzymes of microorganisms.

Furthermore, the mode of action of the compounds may involve formation of hydrogen bond through azomethine group with the active centres of cell constituents, resulting in interference with the normal cell process.[46]

A comparative study of MIC values of the Schiff base ligands and their complexes against the microorganism *Escherichia coli* is listed in Table IV. Analysis of MIC values revealed that most of the complexes show appreciable antibacterial activity. Many complexes are twofold more potent than the ligands and a very few complexes are four fold more potent than the ligands against the bacteria *E.coli*.[47]

CONCLUSION

The work described in this paper involved syntheses and characterization of a series of cobalt, nickel, copper, zinc and cadmium complexes with the Knoevenagal β-keto ester Schiff bases derived from S-methyl dithiocarbazate and [(HPOB--(HSMD)$_2$], [HEOA--(HSMD)$_2$] and [(HMOA---(HSMD)$_2$]. These complexes were characterised by different physicochemical techniques. These complexes are neutral and found to have a square planar geometry with the four donor atoms of the ligand. The synthesised complexes have antibacterial and antifungal activity against *S.aureus*, *E. coli* and *C. albicans* and *A. niger* .Unlike the Knoevenagal β- keto ester Schiff base ligands, the complexes showed good antibacterial and antifungal activity.

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Source of Support: Nil, **Conflict of Interest:** None.